In the Claims:

Please amend the claims, as follows:

47. (Twice amended) A process of screening a substance for its ability to interact with an opioid receptor, said process comprising the steps of:

a) providing an [a] opioid receptor polypeptide wherein said opioid receptor polypeptide is selected from the group consisting of: (1) chimeric opioid receptors, (2) recombinant opioid receptor polypeptides, wherein said opioid receptor polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:1 [including the amino acid sequence of SEQ ID NO:2] and (3) recombinant opioid receptor polypeptides, wherein said opioid receptor polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:11 [including the sequence of SEQ ID NO:12];

b) contacting said substance with the opioid receptor polypeptide; and

c) detecting the ability of said substance to interact with said opioid receptor.

49. (Twice amended) The process of claim 48, wherein one polypeptide of the chimeric opioid receptor polypeptide comprises the second extracellular loop of kappa [delta] opioid receptor.

59. (Twice amended) A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is selected from the group consisting of: (1) chimeric opioid receptors, (2) recombinant opioid receptor polypeptides, wherein said opioid receptor polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous

bases of SEQ ID NO:1 [including the amino acid sequence of SEQ ID NO:2] and (3) recombinant opioid receptor polypeptides, wherein said opioid receptor polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:11 [including the sequence of SEQ ID NO:12];

b) contacting said opioid receptor polypeptide with a composition comprising said candidate substance;

c) detecting the ability of said candidate substance to specifically interact as an agonist with said opioid receptor; and

d) isolating said substance if the ability of said candidate substance to specifically interact with the opioid receptor is detected.

84. (Amended) A process of screening a substance for its ability to interact with an opioid receptor, said process comprising the steps of:

a) providing an [a] opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence [polynucleotide] comprising a base sequence that is identical or complementary to a segment of at least 30 [40] contiguous bases of SEQ ID NO:1 or SEQ ID NO:11;

b) contacting said substance with the opioid receptor polypeptide; and

c) detecting the ability of said substance to interact with said opioid receptor.

Please add the following claims:

--91. A process of screening a substance for its ability to interact with an opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:1;

b) contacting said substance with the opioid receptor polypeptide; and

c) detecting the ability of said substance to interact with said opioid receptor.

92. The process of claim 91, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:1.

93. The process of claim 92, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 50 contiguous bases of SEQ ID NO:1.

94. The process of claim 93, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 75 contiguous bases of SEQ ID NO:1.

95. The process of claim 94, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 100 contiguous bases of SEQ ID NO:1.

96. The process of claim 95, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 680 contiguous bases of SEQ ID NO:1.

97. A process of screening a substance for its ability to interact with an opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said substance with the opioid receptor polypeptide; and

c) detecting the ability of said substance to interact with said opioid receptor.

98. The process of claim 97, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:11.

99. The process of claim 98, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 50 contiguous bases of SEQ ID NO:11.

100. The process of claim 99, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 75 contiguous bases of SEQ ID NO:11.

101. The process of claim 100, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 100 contiguous bases of SEQ ID NO:11.

102. The process of claim 101, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 680 contiguous bases of SEQ ID NO:11.

103. A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:1;

b) contacting said opioid receptor polypeptide with a composition comprising said candidate substance;

c) detecting the ability of said candidate substance to specifically interact as an agonist with said opioid receptor; and

d) isolating said substance if the ability of said candidate substance to specifically interact with the opioid receptor is detected.

104. The process of claim 103, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:1.

105. The process of claim 104, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 50 contiguous bases of SEQ ID NO:1.

106. The process of claim 105, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 75 contiguous bases of SEQ ID NO:1.

107. The process of claim 106, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 100 contiguous bases of SEQ ID NO:1.

108. The process of claim 107, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 680 contiguous bases of SEQ ID NO:1.

109. A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said opioid receptor polypeptide with a composition comprising said candidate substance;

c) detecting the ability of said candidate substance to specifically interact as an agonist with said opioid receptor; and

d) isolating said substance if the ability of said candidate substance to specifically interact with the opioid receptor is detected.

110. The process of claim 109, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:11.

111. The process of claim 110, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 50 contiguous bases of SEQ ID NO:11.

112. The process of claim 111, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 75 contiguous bases of SEQ ID NO:11.

113. The process of claim 112, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 100 contiguous bases of SEQ ID NO:11.

114. The process of claim 113, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 680 contiguous bases of SEQ ID NO:11.--

II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

This application was filed May 31, 1995. The application is a divisional application of 08/292,694, filed August 19, 1994, which is currently pending. Claims 1-46 were cancelled and claims 47-80 were added by a Preliminary Amendment. In subsequent prosecution, claims 47-73 and 75-80 were elected following a Restriction Requirement dated October 29, 1996. In a Response to Official Action dated October 27, 1997, claims 53-58, 60-62, and 68-80 were withdrawn from consideration as non-elected species, and claims 81-90 were added. In the Official Action dated June 29, 1998 ("the Action"), claims 47-90 were pending, claims 47-49, 51, 59, 63-67, 81, and 83-90 were rejected, and objections were made to claims 50, 52, and 82. Claims 47, 49, 59, and 84 have been amended in the amendment submitted herewith. Claims 91-

114 have been added in the amendment submitted herewith. Although claims 47-114 are currently pending, only claims 47-52, 59, 63-67, 81-114 are the subject of this response.

Claims 47, 49, 59, and 84 have been amended. Support for these amendments can be found at least at p. 9, lns. 33-35, p. 12, line 30 to p. 13, line 15, p. 34 lns. 8-10, p. 167, lns. 3-4. These amendments do not introduce material for which a new search by the Examiner is required.

Claims 91-114 have been added. Support in the specification for these claims can be found at least at p. 12, line 30 to p. 13, line 30, *inter alia*. Because claims 47, 59, and 84 have been previously examined and their subject matter is similar to the subject matter of the added claims, it is believed that a new search is not required with respect to the added claims.

B. Summary of the Invention

This invention involves Applicants' discovery of a process for screening for substances that interact with an opioid receptor. *See* Specification, p. 18, line 1 to p. 23, line 22 and p. 66 line 19-26, *inter alia*. This process can be accomplished by providing an opioid receptor polypeptide, contacting a candidate substance with the polypeptide, and detecting the ability of the substance to interact with the polypeptide. *See, inter alia*, Specification, p. 18, line 1 to p. 23, line 22 and p. 66, line 27 to p. 76, line 10. This invention has far-reaching implications for identification of substances such as agonists and antagonists of opioid receptors for use in diagnostic, drug design and therapeutic applications.

C. Substitute Declarations

Substitute Declarations are being processed and will be filed in application Serial Number 08/292,694, filed August 19, 1994, from which this present application is a divisional. Copies of this declaration will be submitted once these are executed to correct the priority claim of this application. Foreign priority under 35 U.S.C. §119 (a-d) is not being claimed in this application. Application Serial Number 08/292,694 is a continuation of PCT/US94/05747 filed on May 20, 1994, which is a continuation-in-part of United States Patent Application Serial Number 08/147,592, filed November 5, 1993, which application is a continuation-in-part of United States Patent Application Serial Number 08/066,296, filed May 20, 1993. As can be discerned from the priority claim of the present application, priority is being claimed under 35 U.S.C. § 120 (since the application following the PCT was a continuation under 37 C.F.R. 1.53(b), not nationalization under 35 U.S.C. §371), and therefore, no foreign priority document needs to be submitted in this case, as is indicated on Office Action Summaries dated October 27, 1997 and June 29, 1998.

D. The Title Has Been Amended

The title has been amended to "Methods of Identifying Agonists and Antagonists of Opioid Receptors." The amended title more clearly and accurately describes the invention of the present application, in compliance with 37 C.F.R. 1.72 and MPEP § 606.

E. Claim 59 Is Definite According to 35 U.S.C. § 112, Second Paragraph

The Action rejects claim 59 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. More specifically, the Examiner contends that claim 59 is confusing because it is not clear whether the opioid receptor is contacted with an isolated candidate or a

composition comprising different test compounds. The Examiner also suggests that step d) be amended.

Applicants traverse that the claim is unclear. "The primary purpose of this requirement if definiteness of claim language is to ensure that the scope of the claim is clear so the public is informed of the boundaries of what constitutes infringement of the patent." MPEP § 2173, at 2100-163 (7th ed.). Applicants contend that there is nothing indefinite about the claim, and the claim is not confusing, as the Action contends, just because the claim can be read to employ either an isolated compound or a composition comprising multiple candidates. In fact, this reading of the claim indicates it is not confusing. The claim does not contain a limitation with respect to the candidate substance; however, the scope of the claim is clear as each step of the process is precisely pointed out. Therefore, Applicants respectfully request that this claim is definite and that the rejection be withdrawn.

F. Claims 47-49, 51, 81, 83, and 84-90 Are Enabled According to § 112, First Paragraph

The Action rejected claims 47-49, 51, 81, 83, and 84-90 under 35 U.S.C. § 112, first paragraph because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. The specification, while enabling for specific regions of specific opioid receptors, allegedly does not reasonably provide enablement for any chimeric opioid receptor or any opioid receptor peptides. Applicants respectfully disagree.

The standard for enablement is whether the specification teaches "those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). In the examples,

such as Example 10, one of skill in the art is taught not only a particular domain that can be useful for identifying specific agonists or antagonists but also how such domains or areas within an opioid receptor can be found. Furthermore, as the Action admits, at least two such regions were identified. These domains could be used, as the specification indicates, for a chimeric opioid receptor or as a truncated opioid receptor polypeptide. *See* Specification, for example, at 168, lines 19-35 and p. 170, lines 19-32. The disclosure sufficiently teaches the full scope of the claim, as one of skill in the art could use this disclosure to practice the claimed invention. "That claims are interpreted in light of the specification does not mean that everything in the specification must be read into the claims." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 957, 220 U.S.P.Q. 592, 597 (Fed. Cir. 1983). The claims are not required to be limited solely to those preferred embodiments specifically disclosed in the description of the invention. *See In re Goffe,* 542 F.2d 564, 191 U.S.P.Q. 429 (CCPA 1976) ("To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for 'preferred' materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts."). Therefore, Applicants contend that the claims are enabled for the use of both chimeric opioid receptors and opioid receptor polypeptides and fragments, and request that this rejection be withdrawn.

G. Claims 59 and 63-67 Are Enabled in Accordance with 35 U.S.C. § 112, First Paragraph

Claims 59 and 63-67 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. First, the Action contends that the

claims are presently directed to a method of isolating a substance that is a specific agonist of a kappa opioid receptor, but that the recited process steps require the use of the substance in isolated form, which is not a limitation in the claim. Second, the Action alleges that the claim is directed to a process for identifying agonists of the kappa opioid receptor and recites a step wherein any chimeric opioid receptor is provided, but that the specification teaches that a specific loop of the kappa opioid receptor is required for a specific ligand interaction. The rejection is inaccurate on both grounds.

Applicants respectfully traverse the first basis for asserting this rejection based on 35 U.S.C. § 112, first paragraph. The Action alleges that step b) of the recited process must be performed with an isolated substance in order for the skilled artisan to determine whether a substance is a specific agonist of a kappa opioid receptor. If the candidate substance of step b) were not an isolated compound or a composition comprising several candidates, the skilled artisan would not be able to determine which compound is an agonist for the kappa opioid receptor. Applicants contend that one of skill in the art is well capable of determining which of several candidate compounds is a specific agonist of a kappa opioid receptor even if an isolated compound was not used in the screening method. Since a skilled artisan could provide a compound that is isolated prior to it being screened for an interaction with a kappa opioid receptor, a skilled artisan could isolate the compound subsequent to it being screened for an interaction. The only difference is that the skilled artisan would be aware of the compound's interaction with the receptor before isolation methods were employed, and in fact, the interaction could be used as an assay throughout the isolation process.

Alternatively, the claimed invention covers screening a composition that could contain a number of already isolated compounds, as a way of increasing the efficiency of the screen. If an

interaction between the composition and the receptor is detected, the individual compound could be identified by using the interaction as an assay to test the isolated compounds.

Applicants do not believe that the second basis for the rejection of claims 59 and 63-67 under 35 U.S.C. § 112, first paragraph, is valid.

H. Claims 47, 59, and 84-90 Are Not Anticipated by Ahmed, *et al.*

Claims 47, 59, and 84-90 were rejected under 35 U.S.C. § 102(b) as being anticipated by Ahmed *et al.* The Action relies in part on an argument made in paragraph 10 of the Office Action dated September 17, 1997 in which Ahmed was said to disclose a method of screening for ligands that interact with the human kappa opioid receptor. That Office Action also contended that the method of Ahmed *et al.* comprised providing purified human kappa opioid receptor, incubating the purified receptor with labelled ligands, and detecting the binding of the ligand to the kappa opioid receptor. The present Action further argues that claims 84-90 are anticipated because they encompass the use of the full-length human opioid receptor and because the sequences of the mouse and human opioid receptors have high sequence identity. Applicants traverse the basis for this rejection with respect to each of the rejected claims.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Claim 59 has a step d) of "isolating said substance if the ability of said substance to interact with the opioid receptor is detected." This element is completely absent from the reference. Applicants contend that a proper rejection under 35 U.S.C. § 102(b) has not been made, and thus, request that the rejection of claim 59 as being anticipated be withdrawn.

Furthermore, claims 47 and 59 have been amended to recite the use of an opioid receptor polypeptide, wherein the polypeptide is selected from the group consisting of: (1) chimeric opioid receptors, (2) recombinant opioid receptor polypeptides, wherein the polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of either SEQ ID NO:1 or SEQ ID NO:11. Claims 84-90 are directed to a screening process using an opioid receptor polypeptide that is encoded for by a nucleic acid sequence including a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:1 or NO:11. The anticipation rejection is meritless because step a) recites an opioid receptor polypeptide that is encoded for by a nucleic acid sequence. Nowhere in the Ahmed *et al.* reference is a nucleotide sequence mentioned. Moreover, a nucleotide sequence is not an inherent characteristic of a protein, even if sequenced, because of the degeneracy of the code. *See In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). In this case, the protein was not disclosed as an amino acid sequence, and the authors admitted the protein had not been purified to homogeneity. Nucleic acid sequences could not be derived from the information disclosed in the Ahmed reference.

Furthermore, Applicants note that claims reciting the sequences of at least 40 contiguous bases from SEQ ID NO:1 and a polynucleotide including the base sequence of SEQ ID NO:11 have been allowed in co-pending application Ser. No. 08/147,592. Insofar as the present claims embody methods using the novel and patentable compositions of Ser. No. 08/147,592, these present claims are equally allowable. Therefore, anticipation is not an appropriate rejection because all of the limitations of these claims have not been disclosed by the cited reference of

Ahmed *et al.* Applicants respectfully request that the rejection of claims 84-90 as anticipated by Ahmed *et al.* be withdrawn.

I. Claims 47 and 48 Are Nonobvious over Evans *et al.*

The Action rejects claims 47 and 48 under 35 U.S.C. § 103(a) as being unpatentable over Evans *et al.* The Examiner states that the claims encompass the use of a chimeric opioid receptor comprising a portion of the delta opioid receptor in a ligand screening assay but that the claims as they stand are not limited to chimeric receptors having specific amino acid sequences of the delta opioid receptor. The Action admits that neither of the cited references discloses chimeric delta opioid receptor, but says that the combination of the two references provides motivation and reasonable expectation of success in obtaining chimeric delta opioid receptors. The Action further states that Evans discloses the primary structure of the delta opioid receptor and that Frielle teaches method steps for obtaining chimeric G-protein coupled receptors and using them in ligand binding assays for determining the structure/function relationship of the receptor. Based on these two references, the Action concludes that it would have been *prima facie* obvious to the skilled artisan at the time the invention was made to modify the delta opioid receptor of Evans by following the teachings of Frielle to obtain chimeric delta opioid polypeptides and to use then use them in ligand binding assays to determine which region of the delta opioid receptor is essential for specific ligand binding. Applicants respectfully traverse.

Three basic criteria must be met for an action to establish a *prima facie* case of obviousness:

(1) "there must be some suggestion of motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings";

(2) "there must be a reasonable expectation of success"; and,

(3) "the prior art reference (or references when combined) must teach or suggest all the claim limitations."
MPEP §2142.

Applicant respectfully asserts that all three criteria have not been satisfied in the present case. First, Applicant contends that the Action has failed to present a valid *prima facie* case of obviousness because it has not demonstrated that there exists some suggestion or motivation to combine the teachings of Evans and Frielle, either in the references themselves or in the knowledge of one of ordinary skill in the art. Also, the Action does not establish that there would be a reasonable expectation of success of the invention based on these two references. Finally, the Action does not show how the cited references teach or suggest all of the claim limitations of claims 47 and 48. Therefore, as discussed below, the rejected claims are not obvious in view of Evans and Frielle.

1. There is no suggestion or motivation in either Evans or Frielle to combine their teachings.

Nowhere in any of the references is there any suggestion or motivation to combine their teachings. Evans, which discloses the sequence of a delta opioid receptor, does not mention chimeric opioid receptors; Frielle, which discusses chimeric adrenergic receptors, does not mention opioid receptors. Therefore, the Applicants do not believe that a valid *prima facie* case has been established because the Action does not indicate otherwise, except for a conclusory statement that it would have been *prima facie* obvious to combine the teachings. Moreover, the Board of Patent Appeals and Interferences has held that the fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish obviousness. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (BPAI 1993). Section 2143.01 of the MPEP explains the *Levengood* holding as follows:

> A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references.
>
> MPEP § 2143.01, page 2100-112 (Seventh Ed.).

Furthermore, the fact that a reference or references can be combined or modified is not sufficient to establish obviousness. For example, the Federal Circuit held in *In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990), that the mere fact that combination or modification of a reference or references is possible does not establish obviousness of the resultant combination unless the prior art also suggests the desirability of the combination, *i.e.*, unless the prior art provides motivation to produce the resultant combination. *Id.*; *see also* MPEP § 2143.01, page 2100-91. Therefore, Applicants believe this criterion has not been met, and consequently, a proper *prima facie* case of obviousness has not been established.

2. One of skill in the art would not have a reasonable expectation of using chimeric opioid receptors in the claimed invention.

Not only do Evans and Frielle fail to mention chimeric opioid receptors that could be used in a process for screening a substance for its ability to interact with an opioid receptor, but also these references do not provide a reasonable expectation of success for that invention. The second criterion for a valid *prima facie* obviousness rejection is conspicuously absent. The Frielle reference makes a number of comments about the domains that can be used to construct chimeric adrenergic receptors, but not with respect to any domains of a opioid receptor. One of ordinary skill in the art would have not have a reasonable expectation of success based on these references.

3. Evans and Frielle do not teach all of the claim limitations.

A proper rejection of claims for obviousness over the prior art requires that the references either teach or suggest all the limitation of the claimed invention. The Action has cited Evans and Frielle as rendering the claims unpatentable for being obvious. In this case, however, there appears to be no suggestion in any of these references to use an opioid receptor polypeptide in a process of screening a substance for its ability to interact with an opioid receptor. Moreover, these references do not say anything about using chimeric opioid receptors or receptors whose amino acid sequence includes SEQ ID NO:2 or NO:12. It is well settled patent law that "obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." MPEP §2143.01; *see also In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 351 (Fed. Cir. 1992). Even by the Action's own characterization of the cited references, the entire claimed invention is not described in the collective teachings of Evans and Frielle. Therefore, the rejection of the patentability of the claims for obviousness is erroneous and inappropriate, and Applicant respectfully requests this reason be withdrawn.

4. The references do not provide a reasonable expectation of success of producing the claimed invention and constitute, at best, the basis for an improper "obvious to try" argument.

Finally, Applicant contends that, at best, the references of Evans and Frielle constitute an improper "obvious to try" grounds for rejection. *See Jones v. Hardy,* 220 USPQ 1021, 1026 (Fed. Cir. 1984). According to *In re Eli Lilly & Co.,* 14 USPQ 2d 1741, 1743 (Fed. Cir. 1990), "[a]n 'obvious to try' situation exists when...further investigation might be done as a result of the

disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result or indicate that the claimed result would be obtained if certain directions were pursued." In this case the individual references nor their combination offer a sufficient teaching of employing in a screening process either a chimeric opioid receptor or an opioid receptor polypeptide containing the amino acid sequence of SEQ ID NO:2 or NO:12. Because an "obvious to try" standard is not the proper standard under 35 U.S.C. § 103, Applicants respectfully request the rejection under this section be withdrawn.

J. Claims 50, 52, and 82 Are Not Objectionable

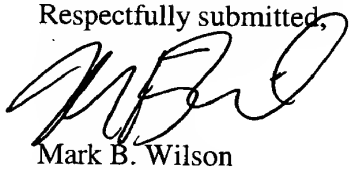
Claims 50, 52, and 82 were objected to as depending from a rejected base claim. Applicants believe the claims upon which they depend have been placed in condition for allowance and respectfully request that this objection be withdrawn.

K. Conclusion

Applicant has submitted remarks that are believed to place the present claims in condition for allowance. In view of this, Applicant respectfully requests that the present claims be passed for allowance. Should the Examiner have any comments or questions with regard to any statements contained herein, or any suggestions as to claim modification, the Examiner is respectfully requested to contact the Applicant's representative listed below.

Please date-stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,



Mark B. Wilson
Reg. No. 37,259
Attorney for Applicant

ARNOLD, WHITE & DURKEE
P.O. Box 4433
Houston, Texas 77210-4433
(512) 418-3000

Date: July 6, 1999

47. A process of screening a substance for its ability to interact with an opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is selected from the group consisting of: (1) chimeric opioid receptors, (2) recombinant opioid receptor polypeptides, wherein said opioid receptor polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:1 and (3) recombinant opioid receptor polypeptides, wherein said opioid receptor polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said substance with the opioid receptor polypeptide; and

c) detecting the ability of said substance to interact with said opioid receptor.

48. The process according to claim 47, wherein said opioid receptor polypeptide is a chimeric opioid receptor polypeptide.

49. The process of claim 48, wherein one polypeptide of the chimeric opioid receptor polypeptide comprises the second extracellular loop of kappa opioid receptor.

50. The process of claim 48, wherein one polypeptide of the chimeric opioid receptor polypeptide comprises the third extracellular loop of kappa opioid receptor.

51. The process of claim 48, wherein the chimeric opioid receptor polypeptide comprises polypeptide portions of both kappa and delta opioid receptors.

52. The process according to claim 48, wherein said chimeric opioid receptor polypeptide is designated as $\kappa_{1\text{-}78}/\delta_{70\text{-}372}$ or $\delta_{1\text{-}69}/\kappa_{79\text{-}380}$.

53-58. [Withdrawn as to non-elected invention]

59. A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is selected from the group consisting of: (1) chimeric opioid receptors, (2) recombinant opioid receptor polypeptides, wherein said opioid receptor polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:1 and (3) recombinant opioid receptor polypeptides, wherein said opioid receptor polypeptides are encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said opioid receptor polypeptide with a composition comprising said candidate substance;

c) detecting the ability of said candidate substance to specifically interact as an agonist with said opioid receptor; and

d) isolating said substance if the ability of said candidate substance to specifically interact with the opioid receptor is detected.

60-62. [Withdrawn as to non-elected invention]

63. The process of claim 59, wherein the opioid receptor polypeptide comprises a chimeric opioid receptor polypeptide.

64. The process of claim 63, wherein one polypeptide of the chimeric opioid receptor polypeptide comprises the second extracellular loop of kappa opioid receptor.

65. The process of claim 63, wherein one polypeptide of the chimeric opioid receptor polypeptide comprises the third extracellular loop of delta opioid receptor.

66. The process of claim 63, wherein the polypeptide comprises portions of both kappa and delta opioid receptors.

67. The process of claim 63, wherein said chimeric polypeptide is designated as $\kappa_{1\text{-}78}/\delta_{70\text{-}372}$ or $\delta_{1\text{-}69}/\kappa_{79\text{-}380}$.

68-80. [Withdrawn as to non-elected invention]

81. The process according to claim 47, wherein said opioid receptor polypeptide is a kappa opioid receptor polypeptide having the sequence of SEQ ID NO:2 or SEQ ID NO:12.

82. The process of claim 81, wherein said opioid receptor polypeptide is a kappa opioid receptor polypeptide encoded for by the polynucleotide of SEQ ID NO: 1.

83. The process of claim 81, wherein said opioid receptor polypeptide is a kappa opioid receptor polypeptide encoded for by the polynucleotide of SEQ ID NO: 11.

84. A process of screening a substance for its ability to interact with an opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:1 or SEQ ID NO:11;

b) contacting said substance with the opioid receptor polypeptide; and

c) detecting the ability of said substance to interact with said opioid receptor.

85. The process of claim 84, wherein said polynucleotide comprises a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:1.

86. The process of claim 84, wherein said polynucleotide comprises a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:11.

87. The process of claim 84, wherein said polynucleotide comprises a base sequence that is identical or complementary to a segment of at least 55 contiguous bases of SEQ ID NO:1.

88. The process of claim 84, wherein said polynucleotide comprises a base sequence that is identical or complementary to a segment of at least 55 contiguous bases of SEQ ID NO:11.

89. The process of claim 84, wherein said polynucleotide comprises a base sequence that is identical or complementary to a segment of at least 70 contiguous bases of SEQ ID NO:1.

90. The process of claim 84, wherein said polynucleotide comprises a base sequence that is identical or complementary to a segment of at least 70 contiguous bases of SEQ ID NO:11.

91. A process of screening a substance for its ability to interact with an opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:1;

b) contacting said substance with the opioid receptor polypeptide; and

c) detecting the ability of said substance to interact with said opioid receptor.

92. The process of claim 91, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:1.

93. The process of claim 92, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 50 contiguous bases of SEQ ID NO:1.

94. The process of claim 93, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 75 contiguous bases of SEQ ID NO:1.

95. The process of claim 94, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 100 contiguous bases of SEQ ID NO:1.

96. The process of claim 95, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 680 contiguous bases of SEQ ID NO:1.

97. A process of screening a substance for its ability to interact with an opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said substance with the opioid receptor polypeptide; and

c) detecting the ability of said substance to interact with said opioid receptor.

98. The process of claim 97, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:11.

99. The process of claim 98, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 50 contiguous bases of SEQ ID NO:11.

100. The process of claim 99, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 75 contiguous bases of SEQ ID NO:11.

101. The process of claim 100, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 100 contiguous bases of SEQ ID NO:11.

102. The process of claim 101, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 680 contiguous bases of SEQ ID NO:11.

103. A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:1;

b) contacting said opioid receptor polypeptide with a composition comprising said candidate substance;

c) detecting the ability of said candidate substance to specifically interact as an agonist with said opioid receptor; and

d) isolating said substance if the ability of said candidate substance to specifically interact with the opioid receptor is detected.

104. The process of claim 103, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:1.

105. The process of claim 104, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 50 contiguous bases of SEQ ID NO:1.

106. The process of claim 105, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 75 contiguous bases of SEQ ID NO:1.

107. The process of claim 106, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 100 contiguous bases of SEQ ID NO:1.

108. The process of claim 107, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 680 contiguous bases of SEQ ID NO:1.

109. A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

a) providing an opioid receptor polypeptide wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is

identical or complementary to a segment of at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said opioid receptor polypeptide with a composition comprising said candidate substance;

c) detecting the ability of said candidate substance to specifically interact as an agonist with said opioid receptor; and

d) isolating said substance if the ability of said candidate substance to specifically interact with the opioid receptor is detected.

110. The process of claim 109, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 40 contiguous bases of SEQ ID NO:11.

111. The process of claim 110, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 50 contiguous bases of SEQ ID NO:11.

112. The process of claim 111, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 75 contiguous bases of SEQ ID NO:11.

113. The process of claim 112, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 100 contiguous bases of SEQ ID NO:11.

114. The process of claim 113, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising a base sequence that is identical or complementary to a segment of at least 680 contiguous bases of SEQ ID NO:11.